REMARKS

The present invention relates to immunological latex turbidimetry method and reagent.

In the Office Action dated March 30, 2005, claims 1-10 were rejected. It is appreciated that Examiner has acknowledged receipt considered of Applicants' Information Disclosure Statements filed on January 30, 2002 and February 17, 2005.

The Examiner has objected to the specification at page 4, with respect to the spelling of "trypsin" (correct) and to the Abstract as containing more than one paragraph.

Claims 1-10 have been rejected under 35 U.S.C. § 112, second paragraph, particularly with respect to the use of the term "carrying" in claims 1 and 6; the Examiner raised the question as to whether it might be more appropriate to use a term such as "comprising" or "consisting of".

Turning to the prior art, claim 6-9 were rejected under 35 U.S.C. § 102(b) based on U.S. Patent 4, 427,781 (Masson et al). Claim 10 has been rejected under 35 U.S.C. § 103(a) based on Masson et al in view of Nakase et al. Claims 1-5 have been rejected under § 103(a) based on Kojima et al in view of Masson et al and further in view of Nakase et al.

In response to the Office Action, Applicants have herein amended the paragraph at page 4 of the specification to correct the spelling of "trypsin", and the Abstract of the Disclosure has been amended to improve the form thereof and place it in a single paragraph.

Accordingly, it is respectfully submitted that the objections to the specification and Abstract have been overcome.

Independent claims 1 and 6 have been amended to more specifically indicate that the sample containing the antigen or antibody to be analyzed in step (1) is brought into contact with a protease-treated bovine serum albumin. Accordingly, claims 2, 3, 7, and 8 have been canceled.

For the reasons discussed below, it is respectfully submitted that in accordance with the present Amendment, remaining claims 1, 4-6, and 9-10 are now in condition for allowance.

First, with respect to the rejection of independent claims 1 and 6 under § 112, second paragraph, Applicants appreciate the Examiner's suggestions of the possibility of using a term such as "comprising" or "consisting of" in claims 1 and 6. However, Applicants respectfully submit that the term "carrying" presently set forth in claims 1 and 6 is technically a more appropriate term than a term such as "comprising" in the recitation "latex particles *carrying* an antibody or antigen. Particularly, if, for instance, the term "comprising" was to be used, such term might be considered to allow for the antibody or antigen to be inside of the latex particle. On the other hand, Applicants respectfully submit that the term "carrying" more clearly indicates

that the antibody or antigen would be carried on the surface of the latex particle. Therefore, Applicants respectfully submit that the term "carrying" is appropriate in claims 1 and 6, and respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Below, Applicants respectfully address the issue of the prior art rejections, and explain why the present invention in accordance with amended remaining claims 1, 4-6, and 9-10 distinguish over the cited art such that the prior art rejections should now be withdrawn, and the remaining claims allowed forthwith.

Rejections under 35 U.S.C. § 102(b) and § 103(a)

(1) Characteristic features of the present invention

One important feature of the present invention resides in, but is not limited to, that (i) a protease-treated bovine serum albumin (BSA) is used as an agent for reducing a non-specific reaction in an immunological latex turbidimetry analysis (page 3, lines 7-3 from the bottom of the present specification). More particularly, before a sample to be analyzed is brought into contact with latex particles, the sample is brought into contact with the protease-treated bovine serum albumin, also referred to herein as BSA (page 5, lines 21-25). According to the feature (i) of the present invention, measurement errors due to non-specific reactions can be decreased (page 15, lines 8-6 from the bottom).

The advantageous effect obtained by the protease-treated BSA was first found by the present inventors, and the feature (i) of the present invention and the advantageous effect

obtained thereby are not disclosed or suggested in the following references cited in the Office Action.

(2) Masson et al reference (U.S. Patent 4,427,781)

In the Office Action (at page 4, lines 1-2) it was indicated that "Masson et al teach a reagent comprising protease-treated albumin and antigen-coated particles." However, Applicants submit that the protease-treated albumin, particularly the "protease-treated BSA" in accordance with the present invention, is not disclosed or suggested in the Masson et al reference, as is further explained below.

In the EXAMPLE of the Masson et al reference, as a latex reagent for assaying anti-digoxin IgG, latex particles carrying a BSA-digoxin conjugate (hereinafter referred to as "digoxin-BSA-latex") are disclosed (column 5, lines 44-60). Further, the Masson et al reference discloses an assay of anti-digoxin IgG in human sera using digoxin-BSA-latex (column 5, line 3 from the bottom to column 6, line 55), and the procedure of the assay is described as follows:

> "Digoxin was dissolved in ethanol to a concentration of 1 g/L. To prepare the standards, this solution was then diluted with a pool of normal human sera....Samples of about 200 µl were mixed with 100 µl of Freon 113 (...) while vortexing and then centrifuged for 5 min at 5000 rev/min. For protease digestion of the samples (to destroy proteins), aliquots of about 100 µl of the clear supernatants were incubated for 10 min at 37°C with 300 µl HCL-pepsin. The digestion was then stopped by addition of 20 µl of 2 mol/1TRIS (tris (hydroxymethyl) methylamine). Protease digestion was also applied, in exactly the same manner, to the standards.
> ...approximately 200 µl, of treated serum was pipetted into a sample tube 11 and placed in the inner row of the sampler tray. A probe from station 12 aspirates 100 µl of the sample into another

> sample tube (called a reaction tube), then 15 μl of the agglutinating mixture and 15 μl of latex conjugate were subquentially at stations 13 and 14. After incubation at 37 °C for 25 min in the vortexing tray...the resulting stream passed through the optical cell counter (3)." (column 5, line 3 from the bottom to column 6, line 55)

As described above, in the assay disclosed in the Masson et al reference, after samples to be analyzed (i.e., human sera) were digested with pepsin for 10 min and the digestion was stopped by addition of TRIS, the pepsin-treated serum samples were brought into contact with the digoxin-BSA-latex to cause a latex agglutination reaction.

As is well-known, pepsin acts under acidic conditions, but does not act under neutral or alkaline conditions. Therefore, when the digoxin-BSA-latex is mixed with the pepsin-treated serum sample, in the presence of the agglutinating mixture(*2) of approximately pH 9.2, BSA carried on the latex is not digested with the pepsin contained in the pepsin-treated serum sample. Thus, "protease-treated BSA" is not generated (i.e., does not exist) in the assay system disclosed in the Masson et al reference.

> [(*2): As described in column 5, lines 19-40 of the Masson et al reference, the agglutinating mixture was prepared by mixing anti-digoxin IgG with RF (rheumatoid factor) and GBS-BSA (a solution of BSA dissolved in glycine buffered saline, pH 9.2).]

As described above, it is seen that the presently claimed invention is clearly different from the assay disclosed in the Masson et al reference with respect to the use of "protease-treated BSA" [i.e., the above feature (i) of the present invention]. Furthermore, the advantageous effect

obtained by the feature (i) of the present invention, i.e., the effect that an error measurement due to the non-specific reaction can be decreased, is not disclosed or suggested in the Masson et al reference. Therefore, Applicants respectfully submit that the present invention exhibiting such an advantageous effect would not be obvious from the disclosure of the Masson et al reference.

(3) Nakase et al reference (JP 48019719) and Kojima et al reference (JP 07140145)

As pointed out by the Examiner, the Nakase et al reference discloses that the addition of BSA to streptolysin O stabilizes streptolysin O. Further, as pointed out by the Examiner, the Kojima et al reference discloses tubidimetric assays for anti-streptolysin O antibodies.

However, neither of the Nakase et al nor the Kojima et al references discloses or suggests the above feature (i) of the present invention and the advantageous effect obtained by the feature (i).

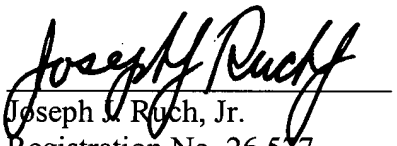
In view of the foregoing amendments and remarks, Applicants respectfully submit that the rejections should now be withdrawn, and remaining claims 1, 4-6, and 9-10 should be allowed forthwith.

Early favorable action is earnestly solicited.

If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned attorney at the local Washington, D.C. telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



Joseph J. Ruch, Jr.
Registration No. 26,577

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

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